

Remarks

Claims 22-39 are pending in the subject application. By this Amendment, Applicants have amended claim 22. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 22-39 are currently before the Examiner and read on the elected invention. Favorable consideration of the pending claims is respectfully requested.

At the outset, Applicants request the courtesy of an interview in this matter prior to the issuance of another Office Action as it is believed that it may be possible to resolve any outstanding issues that remain after consideration of the claims presented for examination and the arguments presented herein.

Claims 22-39 are rejected under 35 U.S.C. § 103(a) as obvious over Novick *et al.* (WO 99/09063, 1999) in view of Shibuya *et al.* (U.S. Patent No. 6,406,909) and Ciccarone *et al.* (WO 02/077202, 2002). The Office Action indicates that Novick *et al.* teach production of recombinant IL-18BP in serum-free culture medium and teach use of CHO cells for production but do not teach any components of the serum-free medium. The Office Action states that Shibuya *et al.* teach components of a serum-free medium including asparagine at 32.5 mg/L, sodium selenite at 0.0043 mg/L, and wheat protein hydrolysate at 1g/L. The Office Action cites Ciccarone *et al.* for teaching additional medium components and for teaching a medium that lacks glutamine. Applicants respectfully submit: 1) that a *prima facie* case of obviousness has not been established for the claimed invention; and 2) that the Patent Office has improperly rejected the claimed invention and has failed to consider all the pertinent law related to the “optimization of ranges”.

As the Patent Office is aware, all the claim limitations must be taught or suggested by the prior art in order to establish the *prima facie* obviousness of a claimed invention (*CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) citing *In re Royka*, 490 F.2d 981, 985 (C.C.P.A. 1974)). As noted in the previous response, the amounts of asparagine, selenite and/or wheat hydrolysate recited in the claims are present in amounts that exceed any of the amounts taught or suggested in Shibuya *et al.* and Ciccarone *et al.* (see the previously presented Table, reproduced below).

Component	Claims	Shibuya <i>et al.</i>	Ciccarone <i>et al.</i>
Asparagine	about 800 to about 900 mg/L	32.5-65 mg/L	5-50 mg/L
Wheat Hydrolysate	about 5000 to about 15000 mg/L	500 to about 3000 mg/L	None
Selenite	about 5 to about 15 micrograms/L	4.3 micrograms sodium selenite/L	0.0001 to 0.03 micrograms/L
Insulin	about 2.5 to about 6 mg/L	5 mg/L	10 g/L (if present)
Natrium chloride	about 3000 to about 4500 mg/L	1025 mg/L	600-16000 mg/L

The Final Rejection discusses a pair of the components recited within the claims (natrium chloride (sodium chloride) and insulin and argues that one element from Shibuya *et al.* (insulin) and one element from Ciccarone *et al.* (natrium (sodium) chloride) are disclosed to have overlapping ranges with those claimed herein; however, the concentrations of the other recited components of the medium are not within the ranges taught or suggested by any of the cited prior art references. Thus, it is respectfully submitted that a *prima facie* case of obviousness has not been established for the claimed invention as each of the limitations of the claims is not taught or suggested by the cited combination of references and reconsideration and withdrawal of the rejection is respectfully requested.

In addressing the previously submitted arguments pertaining to the non-obviousness of the claimed invention, the Office Action cites to M.P.E.P §2144.05 for support for the proposition that “differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. ‘[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.’ *In re Aller*, 220 F.2d 454, 456, 105 U.S.P.Q. 233, 235 (C.C.P.A. 1955) see M.P.E.P 2144.05 (paragraph bridging pages 3-4 of the Final Rejection). This passage is found in M.P.E.P §2144.05(II)(A).

Applicants also note that the Office Action does not reference M.P.E.P §2144.05(II)(B) where it is stated:

***B. Only Result-Effective Variables Can Be Optimized***

A particular parameter must first be recognized as a result-effective variable, *i.e.*, a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 U.S.P.Q. 6 (C.C.P.A. 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq. ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable.).

In responding to Applicants' previously filed remarks, the Office Action states "Although the concentrations of asparagine, sodium chloride, selenite, wheat hydrolysate, insulin are not recognized in the prior art as result-effective variables, it would have been well within the ability of one of skill of the art to optimize and the concentrations for each component of the serum free media recited in the claims of the instant application" (see Office Action at page 5, second paragraph). Thus, it is admitted that these elements are not recognized as result effective variables and the Office Action appears to have not considered the admonition within the M.P.E.P. that "[a] particular parameter must first be recognized as a result-effective variable, *i.e.*, a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 U.S.P.Q. 6 (C.C.P.A. 1977)". Applicants further note that the concentrations of several of the medium components (*e.g.*, selenite, wheat hydrolysate and asparagine) are far outside the concentrations taught or suggested by Shibuya *et al.* or Ciccarone *et al.* As noted in the previous response, the Board of Patent Appeals and the predecessor of the Court of Appeals for the Federal Circuit (the Court of Customs and Patent Appeals) have held that while it may generally be a matter of obviousness for the skilled artisan to determine the optimum value within a disclosed range, *In re Boesch*, 617 F.2d 272, 276 (C.C.P.A. 1980), it would not have been obvious for one of ordinary skill in the art to find an optimum value that is far outside the range taught by the prior art. *See In re Sebek*, 465 F.2d 904, 907 (C.C.P.A. 1972). *See also, e.g., Ex parte Atkinson*, Appeal 2007-3900 ("optimization of a known result-effective variable in a given range is generally obvious only when it is reasonably expected that an improvement will arise in that range") (reversing Examiner's optimization-based obviousness rejection; internal citation omitted). Accordingly, it is respectfully submitted that the claimed

invention has been improperly rejected in the Final Rejection and reconsideration and withdrawal of the rejection of record is respectfully requested.

The Office Action also argues (at page 4):

At page 7 of the response, Applicants argue that the medium by Shibuya et al. teaches that glutamine is present in the media disclosed therein and no basis for deleting this component is provided in the Office Action. In addition, Applicants argue that there is not articulated reason in the Office Action to omit glutamine from the media taught by Shibuya et al.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 U.S.P.Q. 871 (C.C.P.A. 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 U.S.P.Q. 375 (Fed. Cir. 1986).

Although the reference by Shibuya et al. does not disclose a motivation to omit glutamine as one of the component of serum free media, the addition or removal of glutamine would have been well within the ability of one of skill in the art to optimize the serum free medium for the cultivation of cells producing IL-18BP.

At the outset, Applicants note that no evidence has been provided establishing that glutamine was recognized in the art as a result-effective variable that one skilled in the art would have been motivated to (or sought to have) modified to optimize cell culture. Applicants also respectfully submit that the Patent Office bears the initial burden of showing unpatentability. See, e.g., *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). “[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006) (quoted in *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct 1727, \_\_\_, 82 USPQ2d 1385, 1396 (2007)). In this case, the Office Actions contain only conclusory statements and have not presented any evidence as to why one skilled in the art would have been motivated to omit glutamine as a component of the medium claimed herein; rather, the Office Action only offers a conclusory statement that “[a]lthough the reference by Shibuya et al. does not disclose a motivation to omit glutamine as one of the component of serum free media, the addition or removal of glutamine would have been well within the ability of one of skill in the art to optimize the serum free medium for the cultivation of cells producing IL-18BP”. Applicants

respectfully submit there has been no articulated rationale for omitting glutamine from the culture medium and that the rejection of record fails to meet the evidentiary requirements for establishing the obviousness of the claimed invention. Accordingly, reconsideration and withdrawal of the rejection of record is respectfully requested.

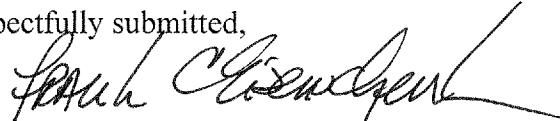
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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